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AN ATTEMPT AT A PHYSIOPATHOLOGICAL EXPLANATION OF SEBORRHOEA AND ACNE VULGARIS: THERAPEUTIC RESULTS.*

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Puberty affects the pilo-sebaceous system of the skin, giving rise to various important changes, including physiological seborrhoea. The process seems in a great measure to be dependent upon the sex hormones. These progressively increase during the puberal period, reaching a maximum at sexual maturity, and play their part in the balance of the various internal secretions; this balance is upset only in certain pathological states.

It is generally recognized that pathological seborrhoea and acne do not occur before puberty, and this justifies the assumption that they are caused by some upset in the hormonal balance. It is, however, by no means easy to explain this disequilibrium. For example, how does it originate? Is it due to the excess, or deficiency, of one or of several secretions? These and many other questions indicate the complexity of the problem. Various contradictions are found when we consider our case-reports in which an attempt has been made to link seborrhoea and acne with possible endocrine factors, whatever the hormone involved—pituitary, thyroid, adrenal or sex.

It is unlikely, however, that a large number of different factors play a part in the aetiology of these disorders. It seems more reasonable to suppose that one morbid condition is produced by a single cause or group of causes. Furthermore, a disorder with similar manifestations in male and female is most likely to have a similar aetiology in the two sexes. This possibility finds expression in the assumption that acne is not due to an anomaly in the secretion of a single hormone, but that it arises from disequilibrium between

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several hormones. Lawrence and Werthessen (1940), Wile (1939), and Jausion (1941, 1944), indeed, as a result of their investigations, concluded that seborrhoea and acne are dependent upon an increase in the value of the ratio $\frac{\text{androgens}}{\text{oestrogens}}$.

This viewpoint explains the similar aetiology of acne in males and females. Furthermore, it takes into account the occurrence of acne in women, associated with either normal or reduced secretion of folliculin. Yet, if this were true, administration of oestrogens would, by re-establishing the $\frac{\text{androgens}}{\text{oestrogens}}$ ratio, have a consistently curative effect. Such is far from being the case.

We treated a series of 64 patients, 50 men and 14 women, with either dienoestrol or ethinyl-oestradiol, in a daily dose of 1 mg. and 0·02 mg. respectively. In women, the courses of treatment lasted 15–20 days (usually from the 8th to the 23rd day of the menstrual cycle) ; courses of 20 days per month were given to the men. The number of courses varied from 1 to 6. In the women we obtained recovery in one and notable improvement in 2 cases as against 11 failures ; in the men we obtained on the whole 70% of cures or marked improvements, of which 30% were achieved after 2 months.

Thus, surprising though it might appear at first sight, the beneficial effect of oestrogens, though inconstant, appears to be greater in men than in women.

The Role of Progesterone.

As early as July 1950 the writer, with Dr. Fitoussi, suggested that another factor might be responsible for upsetting the equilibrium of sex hormones in women, and that this factor might be progesterone. The latter is, indeed, well known to possess an androgenic activity which, according to Selye's (1942) classification, is next to that of testosterone. As was shown by Courrier (1930, 1937, 1941, 1945) and Courrier and Kehl (1938), progesterone is, indeed, a synergist of folliculin in certain circumstances, according to a quantitative ratio, and an antagonist in others.

On the other hand, we had, following the work of Vignes (1937) and Jausion *et al.* (1942), observed the aggravating effect of progesterone on acne eruptions (similar to that of male hormone), whenever we administered the hormone in doses of 20 to 30 mg., in 2 or 3 injections, between the 21st and 25th days of the menstrual cycle.

Accordingly, the acne appeared to us related to a relative or absolute increase in one or other of the terms of the numerator in the ratio :

$$\frac{\text{Androgens} + \text{Progesterone}}{\text{Oestrogens}} \quad \left(\frac{A + P}{OE}\right)$$

Biological Investigations.

Attempt at a Biological Verification.

We attempted to confirm this hypothesis biologically and, in a systematic investigation with our chief Tzanck and with Fitoussi (1950) of the *vaginal cytology* of 58 patients, we found 29 cases of total oestrogenic deficiency, 7 cases of sub-total deficiency, 18 of partial deficiency and 4 normal results. In no case did we find any hyperfolliculinism. Thanks to the close co-operation of some of the patients, we were able to observe that in those women showing a curve of partial deficiency the acne attacks were much more marked during the hypofolliculinic phase of the menstrual cycle.

In 35 patients we were able to compare the urinary excretion of pregnandiol and 17-ketosteroids on the 23rd day of the menstrual cycle with the degree of reaction of the vaginal epithelium to oestrogens. In about half the cases we found, in the ratio $\frac{A+P}{OE}$, a normal or slightly increased numerator and a reduced denominator ; in the other half the oestrogen deficiency was aggravated by a considerable increase in the absolute value of the androgens or progesterone, or of both, with the levels of these reaching, in some cases, 18 mg. for the ketosteroids, and 24 mg. for progesterone.

However, estimation of urinary folliculin, carried out in 12 cases, constantly showed values ranging between the lower limit of normal and the normal average, in contrast with the results obtained from vaginal smears.

The values of folliculostimulin, estimated in 14 cases, were all near the lower limit of normal.

Finally, in 25 investigations the basal metabolic rate was found to be normal in 20, increased in 3, and diminished in 2 cases.

Interpretation.

Thus progesterone may play a part together with the male hormone in the endocrine imbalance of women with acne. We are aware that the results of these investigations have only a relative value, and should be regarded as provisional. Their interest lies in the fact that they throw some light on certain clinical and therapeutic data, which themselves tend to support our assumption. The following are these data :

(i) *Thyroid.*—The secondary role of the thyroid, if it does actually play a role as stated by Cunningham and Lunsford (1931), Sulzberger and co-workers (1934) and Sulzberger and Baer (1949) : apart from an occasional mild tremor or tachycardia, no clinical sign of thyroid dysfunction has ever been confirmed in our investigations of about 300 cases of acne in males and females. In myxoedema the skin is thickened and dry ; in Basedow's disease it is markedly thin.

On the other hand, Rapport and Curtis (1950) found the blood iodine content to be normal in cases of acne.

(ii) *Hypertrichosis.*—Certain cases of virilism with hirsuties are associated with acne, although the excretion of the 17-ketosteroids (which form only part of the androgenic secretion) is normal. An increase in urinary pregnandiol was indeed noted in states of virilism in the adult by Venning and Browne (1947) and Finkler (1947).

(iii) *Premenstrual acne exacerbations.*—Predominance of acne in the second half of the menstrual cycle and, as frequently observed, its aggravation during the early weeks of pregnancy—two stages characterized by progestative secretion.

(iv) *Amenorrhoea.*—Acne does not occur during primary amenorrhoea, but often appears as soon as menstruation has been established.

(v) *Vaginal cytology in acne and amenorrhoea.*—There may be a vaginal cytology similar, but certainly of different significance, in cases of amenorrhoea with no acne and in acne patients who are menstruating normally. The former present no problem ; in these there is indeed an oestrogen insufficiency. In the latter cases, the cytology and the folliculin level do not correspond ; such a discrepancy, which expresses the fact that the patient menstruates, cannot be explained in all cases by a hypothetical lack in receptivity of the vaginal epithelium, particularly since, in every case investigated, we observed the cellular *oestrogen chart* to be altered by treatment. It is probable that this might result from the inhibiting effect exerted by a hypersecretion of an androgen type, particularly progesterone, upon the keratinization of the vaginal mucous membrane. The hypofolliculin tracings in the acne cases might, therefore, be but false indications of oestrogen insufficiency, reflecting in the vaginal epithelium, as acne does in the skin, a disturbance of equilibrium in the ratio $\frac{A + P}{OE}$.

(vi) *Acne and progesterone therapy.*—Finally, the acne-producing effects of progesterone in the dosage we have indicated above may be considered. In this connection it may be objected that Way and Andrews (1950) obtained curative effects from the use of this hormone ; possibly this contradiction may arise because the American authors' dosage was very low compared with ours. Recently, however, Lewis, Frumess and Henschel (1951), repeating the work of Way and Andrews, did not obtain similar satisfactory results.

Nevertheless, such observations have led to the suggestion that the pituitary gonadotropins are involved in the process.

Indeed, there appears to be no question of a total insufficiency of the gonadostimulant secretion, since in Simmonds's disease the skin is waxy, dry and tense. Neither does hypersecretion of folliculostimulin appear to be involved since, on the contrary, castration which causes disappearance of the acne

leads to a significant increase in this hormone. On the other hand, it is admitted that, in the male, oestrogens may inhibit the secretion of luteinizing hormone, whereas in the female they may stimulate it, while at the same time reducing the secretion of folliculostimulin.

Now, in the course of our therapeutic investigations we have observed that chorionic gonadotropin, like progesterone (the secretion of which it stimulates), in a dosage of 2000 to 3000 i.u. administered during the second half of the menstrual cycle consistently aggravates the exacerbations of acne.

By comparing these diverse data one is led to wonder whether the disequilibrium of $\frac{A + P}{OE}$ may not itself be due to a parallel disequilibrium in the hypothalamopituitary mechanisms responsible for the secretion of the sex hormones.

Such a concept would serve to account for—

(i) *Cushing's disease and acromegaly.*—Seborrhoea and acne occur in Cushing's disease together with virilism with hirsuties, in contrast to acromegaly where hirsutism only is present: in acromegaly, indeed, as in Cushing's disease, there is a hypersecretion of corticostimulin, but with a reduction in gonadotropins in most cases.

Furthermore, the disappearance of virilism, seborrhoea and acne following the use of cortisone in those affected with congenital hyperplasia of the adrenals, as observed by Wilkins and co-workers (1951), might, according to Wilkins, be explained by a pituitary mechanism, and might thus result from inhibition of the androgeno-stimulant secretions, luteinizing hormone and ACTH.

According to Bartter *et al.* (1950), who have observed that ACTH does not increase the excretion of the 17-ketosteroids in younger children in whom gonadotropin secretion is low, luteinizing hormone may act in both sexes in synergy with ACTH on the androgenic zone *X* of the adrenal cortex.

(ii) *Oestrogens in men and women.*—Such successful results as we obtained with oestrogen therapy in men are in contrast with failures from the use of the same hormone in women. Again, it may be objected that some authors, such as Goeckerman (1950), Belisario (1951) and Vachon (1951), have obtained good results from the use of the hormone in women, though, again, it is probable that such satisfactory results were due to the use of very low doses as compared with those we employed. These low doses might stimulate secretion of folliculostimulin. This applies in the case of the growth hormone which is stimulated by low doses of folliculin, and, on the contrary, inhibited by large doses (Ferrier (1945), Lichtwitz *et al.* (1949, 1951), Wolfe and Hamilton (1939)).

(iii) *Serum gonadotropins.*—As early as 1932 Max Aron showed experimentally that it is possible, according to the amount of pituitary extract adminis-

tered, to produce either a folliculostimulant effect with low doses, or a luteinizing effect with higher doses. Similar effects were observed by Evans, Simpson and Pencharz (1935), and later by Saunders and Cole (1938), according to the amount of pituitary grafted into hypophysectomized female rats.

On the other hand, it is generally recognized that urinary extracts from menopausal or ovariectomized women possess exclusively folliculostimulant properties, as does pregnant mare's serum (P.M.S.), from which serum gonadotropin is prepared. Frank, Salmon and Friedman (1935) and more recently Hamburger and Pedersen-Bjergaard (1946), using urinary extracts of menopausal women, obtained a folliculostimulant effect with low doses and a luteinizing effect with higher doses.

Treatment with Pregnant Mare's Serum.

The above observations correspond to our own findings with regard to the effect of varying amounts of serum gonadotropin in acne. We have, so far, treated over 230 patients (about half men and half women), 49 by intramuscular injection and the remainder by implantation.* (Tzanck and Aron-Brunetière, 1951; Aron-Brunetière, 1952.)

The injections were at first given for 6 consecutive days, as is usual, during the first half of the menstrual cycle, in a daily dosage of 400–800 i.u. We found, however, that this treatment proved more active and more consistently effective when the injections were given at intervals of 2–3 days in women during the whole intermenstrual period, and in men over periods of 30 days, in a low dosage of from 200–400 units. This encouraged us to try to obtain by implantation a slow and prolonged absorption of the hormone.

Estimating the duration of effect of the implants by the arrest and recurrence of the acne attacks following implantation, we were led to repeat the operation every 20 to 25 days on an average. But, since relapses tend to be more delayed as treatment progresses, as though one obtains not a substitute therapy but a *re-equilibration* of the endocrine balance, the interval may after the second implantation be lengthened by 10 to 15 days. There occurs almost constantly, within two or three days of the implantation, a focal reaction characterized by an exacerbation of the acne which, however, promptly clears up. This seems to correspond to an initial overdose of the hormone. The curative effect of folliculin-stimulant type is not observed until the excess of the nocuous hormone with a lutein-stimulant effect has been eliminated. It is probable that this phenomenon may be responsible for the failures following intramuscular therapy, since this introduces massive doses which are promptly absorbed by the body. It can, therefore, be understood that an overdose from implants might promote a reaction lasting 10–15 days. Accordingly we suggest, as a useful maximum dose, 1000 units in men and 2000 in women.

* The gonadotrophic hormone employed by us was kindly supplied by Laboratoires Roussel.

Results.—By this method, the average of complete cures and marked improvement is almost identical in men and women. This is much higher than that obtained from injection of the hormone : after a lapse of 2 months the injection gives, in both sexes, only 30% success, as against 60% with implantations. This percentage reaches almost 90% when a number of implantations varying from 2 to 6 is given. Most of the patients were followed up for from 2 to 12 months after the last implantation, without any relapse being observed.

In 16 cases (8 men and 8 women) there was a relapse, though of very mild degree compared with the initial cutaneous lesion ; the earliest relapse occurred within 40 days, and the latest 200 days after the end of treatment.

In no case was there any abnormal reaction, either local or general. On the contrary, leucorrhoea (32 cases) and dysmenorrhoea (39 cases) cleared up in 24 and 36 cases respectively ; and—a curious fact—29 out of 31 patients recovered from intractable constipation, which, in 2 cases, reappeared with a recurrence of the dermatosis.

Conclusion.

In pathology one cannot keep to dogmatic values. The present work is merely an outline of the facts personally observed. Nevertheless, the pattern was too consistent to be the result of chance, or devoid of significance. We have attempted to correlate certain conceptions of general physiology with biological, clinical and therapeutic observations. From our findings two sets of facts would appear to emerge, one of theoretical and the other of practical importance.

(i) *Theoretical.*—The facts of theoretical importance appear to confirm the presence of an increase of the ratio $\frac{A}{OE}$ in acne cases and direct attention to the eventual effect of progesterone in the upsetting of this ratio in women. They suggest the possibility of a common origin in the development of acne in both men and women, arising from a relative increase of the lutein-stimulant secretion. Thus, in both sexes a disequilibrium in pituitary gonadostimulins may disturb the balance of the steroid hormones.

This hypothesis, however, does not rule out the operation of other factors. Secondary causes may be added to the endocrine disorder and affect the course of the disease. These Sulzberger has called " chain reactions " : infection which, in many cases, requires a particular treatment either local or general ; the action of vitamins, synergy between which and certain hormones is known to exist ; nervous disorders, for example, the development of acne and seborrhoea observed in cases of epilepsy, encephalitis, etc., might arise from subordination of the pituitary to the infundibulo-tuber-cinerum centres, and may constitute a further indication of the role of the pituitary secretions in the aetiology of acne.

(ii) *Practical.*—The facts of practical importance are :

Firstly, the particular effectiveness of implants of serum gonadotropin, both in men and women ; secondly, the great importance of the amount of the dose, whichever hormone is administered (gonadotropic hormone, folliculin, progesterone). All these hormones appear to be more or less harmful in high dosage, and more or less effective in low dosage.

In support of this work, in which we have been engaged for three years and in which so many points raised require confirmation and should be considered only as indicating further research, the best argument seems to lie in the therapeutic conclusions reached—which we constantly confirm—and which we consider may have a general bearing applicable in other medical fields.

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WERNER'S SYNDROME.

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In 1904 Werner in an M.D. thesis entitled " Cataract in Connection with Sclerodermia " described the syndrome that is now associated with his name. The purpose of this article is to record another case of Werner's syndrome and to distinguish the condition from sclerodermia. A preliminary report will be included on the electronmicroscopic findings in both maladies.

The natural history of Werner's syndrome is fairly constant, and the variations that occur depend on the extent to which each system is involved. The aetiology of the syndrome is not known, so the symptoms will be described chronologically.

The earliest manifestations, which occur in the first and second decades, include precocious whitening of the hair and stunting of growth, which may be accompanied by " loss of flesh " on the feet and to a less extent on the hands.

During the second and third decades the skin becomes atrophic and is stretched over the underlying tissues and bony prominences. There is fine scaling with variable pigmentation ; patchy atrophy and telangiectasia are occasionally present. These changes are most marked on the legs, which look spindly from loss of subcutaneous and muscle tissue. Tightness of skin may cause limitation of ankle movement and produce persistent ulceration over pressure points where there is no protective fat padding (Thannhauser, 1945 ; Schott and Dann, 1949). Circumscribed hyperkeratoses and painful callosities are a distinct feature of the syndrome and are usually situated over the weight-bearing prominences. When removed, they leave a scarred telangiectatic base which frequently becomes ulcerated.

The facies is characterized by beaking of the nose, taut skin over the cheeks, and thick-lensed spectacles ; they are aptly described as " bird-like." Bilateral juvenile cataracts are a constant feature of the syndrome and have a tendency to affect the posterior pole and periphery of the lens. In some cases the voice is high-pitched and husky as a result of thickening and vascularizа-

tion of the vocal cords. Canities becomes associated with calvities, the body, axillary and genital hair is scant and fine, and the nails dystrophic.

The hair and skin changes, as well as cataracts, occur as isolated symptoms in antecedent generations. Dr. E. B. Ford, quoted by Carleton (1943), considered the condition heterozygous, and that other genes were playing a part in determining the expression of the major gene ; there was no evidence of sex linkage or of sex-controlled inheritance. The complete syndrome itself is usually self-limiting and tends to occur in brothers and sisters ; frequently there is a history of consanguinity.

Endocrine upset is varied and includes hypogonadism, insulin resistant diabetes, thyroid dysfunction and hyperparathyroidism (Oppenheimer and Kugel, 1934 ; 1941). Osteoporosis, especially of the lower limbs, and metastatic calcification of muscles, ligaments and arteries may be present. Hyperostosis frontalis interna has been reported in several cases.

Arteriosclerosis may be manifest from the third decade onwards. The association of skin changes with greying and thinning of the hair makes the patient appear prematurely aged, and in combination with the facies, spindly legs, dwarfed stature and hypogonadism, gives a remarkably constant picture to the syndrome.

Case Report.

T. C. R—, a single man aged 48, was admitted to the Geriatric Unit at St. James's Hospital for the treatment of acute congestive heart failure in April 1950. A full history, taken later, revealed that his parents were unrelated, and that his father and great aunt had premature white hair. The patient himself suffered from callosities on his feet since childhood. As a boy he could never remember being able to walk barefoot on the sands because, as his doctor said at the time, " there was not enough flesh on his feet." All his life he has had a high-pitched voice and been of short stature. For the past ten years there has been greying and thinning of the hair and he has looked much older than his age. At the beginning of this period his sexual interest and activity ceased. His skin has become dry and scaling and his feet, formerly hyperidrotic, are now continually dry. Four years ago he had an exostosis excised over the head of the right fifth metatarsal bone. This lesion had been present for nine months. Osteomyelitis developed, his right knee became " fixed " and a mid-thigh amputation was performed five months later. About this time a warty callosity started to develop on the left tendo Achillis. He also noticed that his sight was failing, and three and a half years ago had an operation for cataract on the right eye which restored his vision.

For the past two years he has had progressive dyspnoea on exertion, oedema of the legs and enlargement of the abdomen ; paroxysmal nocturnal dyspnoea and oliguria was present for the two weeks prior to admission.

On examination the patient looked fifteen years older than his age and his voice was high-pitched and husky. His hair was grey and thin on the scalp and pubic region, and was practically absent in the axillae ; none was seen on the body. The skin of the face was shiny with a little increased pigmentation, the cheeks pinched, the nose sharp and the skin of the ears taut and atrophic. The skin of the upper limbs and trunk showed the fine scaling and early wrinkled atrophy of old age. Follicular plugging was seen on the trunk, and especially over the abdomen. The

limbs were wasted (Fig. 1). Over the backs of the thighs and the lower part of the buttocks the changes were more marked and extended to involve the whole of the lower part of the leg; below the knee the skin was pigmented, glossy, covered with atrophic scales, and taut over the wasted underlying subcutaneous tissue and muscle. (The scaling skin extended on the right leg to the end of the lower thigh amputation stump.) On the foot (left) there were telangiectatic changes over the malleoli and the fifth metatarsal head. There was a circumscribed hyperkeratosis on the tendo Achillis measuring $\frac{3}{8}$ in. in diameter. Smaller but painful lesions with erythematous bases were present on the sole over the heads of the first and fifth metatarsal

FIG. 1.—Werner's syndrome with characteristic spindly limbs, small genitalia and premature ageing.

bones. There had been a similar lesion on the heel which left a depressed scarred area $\frac{1}{2}$ in. in diameter. A small indolent ulcer was present on the dorsum of the second toe. The dorsalis pedis and posterior tibial arteries were not palpable. Ankle movement was limited to 15°. The circumferences of the left calf and ankle were $8\frac{1}{4}$ in. and $8\frac{1}{2}$ in. respectively, and that of the forearms and wrists averaged $6\frac{7}{8}$ in. and $5\frac{1}{4}$ in. The patient's height was 5 ft. $1\frac{1}{2}$ in. The penis was small and the testes a little reduced in size (Fig. 1). A post-operative coloboma could be seen superiorly in the right eye, and a dense cataract in the left.

Laryngoscopic examination (Mr. G. Seed) showed the posterior pharyngeal wall to be dry and pale. The vocal cords moved well and showed increased vascularity on their upper surface.

General medical examination revealed the signs of congestive heart failure.

Histological section from the lower part of the left leg (Dr. H. Haber): The epidermis showed atrophy of the stratum spinulosum, the layers being reduced to two or three rows of cells. There was a loose hyperkeratosis of the stratum corneum. The papillary body was stretched, had disappeared entirely in some places and was only slightly outlined in others. On comparison with the atrophic parts some areas could be described as acanthotic. Spongiosis and vesicle formation were present. The basal layer was heavily pigmented in places.

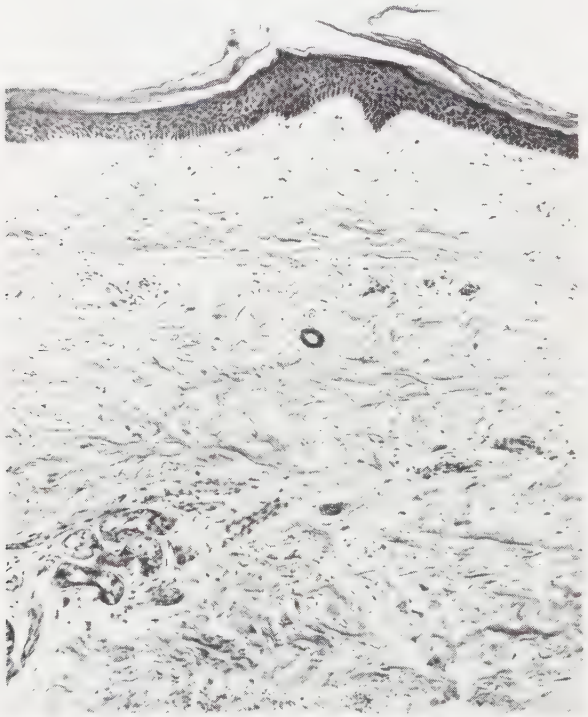

FIG. 2.—Histological section from the lower part of the left leg. The epidermis is atrophic, while in the corium the fibres are thin but have normal tinctorial reactions. H. & E., × 55.

In the corium the bundles were thin, atrophic, and tended to be arranged parallel to the surface. The vessels were normal and no inflammatory change was seen. The pilosebaceous apparatus had disappeared, while the sweat glands were atrophic and their ducts cystically dilated. The elastic stain revealed a very well developed subepidermal garland, and a normal condition throughout the corium. Elastic fibres were not found around the sweat glands.

The histology was that of a hypoplasia and not of a sclerodermia (Fig. 2 and 3).

Skiagrams showed extensive calcification of the tendo Achillis, and minimal osteoporosis of the foot and the lower part of the leg. There was calcification of the vessels and tendons of the lower part of the leg and amputation stump. A plaque of calcification was seen in the aortic arch. Congestive changes were noted in the lungs and there was some cardiac enlargement.

The following tests were carried out with normal results: Complete blood count, blood calcium, phosphorus, cholesterol, acid and alkaline phosphatase, serum bilirubin, glucose tolerance test, urea clearance test, daily urinary excretion of 17-ketosteroids, and electrocardiogram.

Examination of the patient's brother, R. E. R—, revealed certain similar changes. Although only 46 years old he looked at least 60: he showed early senile elastosis of the face and an arcus senilis, and had a moderately high-pitched voice. His penis was small, and he stated he never had any sexual inclinations or activity. The patient's sister, S. R—, aged 50, refused to be examined, but it was noted that she had similar facies. All three were single and lived together.

FIG. 3.—Histological section. Thin collagen bundles can be seen arranged parallel to the surface; the elastic fibres appear normal. Weigert's elastic stain. × 70.

ELECTRON MICROSCOPY.

A small piece of skin was obtained at biopsy from the lower part of the patient's right leg and stored in ice-cold saline. After washing in water the tissue was thoroughly washed with ether to remove any fatty material. From the tissue, which was very firm in texture, small pieces of the dermis were dissected and were further fragmented in a drop of distilled water, using fine sharp knives. Droplets of the suspension so formed were mounted on a thin film of collodion, supported by the conventional type of specimen grid. The preparations were dried and then shadowed with a thin layer of chromium in order to enhance the contrast.

Electron microscopic examination of many portions of the samples are consistent in showing collagen fibrils with much amorphous debris adhering to them (Fig. 4). So much of this debris is present that it is often quite impossible to observe the typical cross-striated appearance of the collagen fibril or, indeed, to say with any certainty whether any of the underlying fibrils

are degenerate. The debris is easily digested by trypsin so that apparently normal collagen fibrils remain (Fig. 5). Tryptic digestion of debris has been carried out in other pathological specimens, e.g., senile elastosis, where in addition the short, bent degenerated fibrils are removed, leaving apparently normal ones. Further work is needed to assess the origin and nature of this

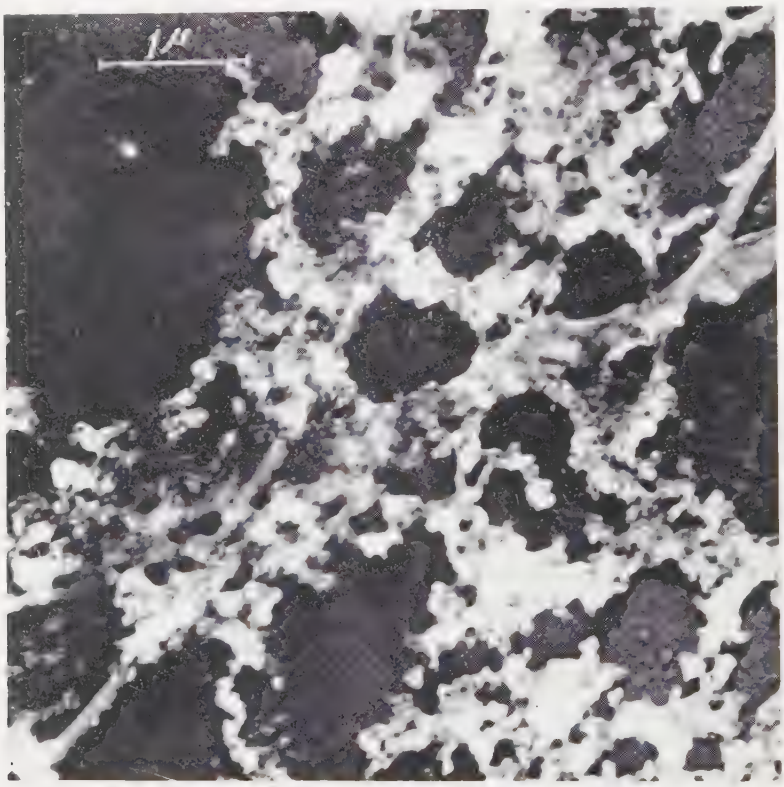

FIG. 4.—Electron micrograph from dermis in Werner's syndrome with granular debris material almost obscuring a collagen fibril. × 14,500.

amorphous debris: all that can be said at present is that it appears to possess a unique granular appearance, in contrast to that observed in many other pathological skin conditions.

Various types of sclerodermia have shown similar changes in the electron micrographs (Figs. 6 and 7) (Seville, 1951; 1952). Briefly, the amorphous debris increases in amount in proportion to the degree of homogenization and swelling seen histologically. The majority of the collagen fibrils appear normal (Fig. 7), but occasionally shortening, bending, fraying of the ends and thinning are observed (Fig. 6). It is hoped to give further details of the significance of these changes in a later paper.

We believe that Werner's syndrome and scleroderma can be differentiated by the appearance of the amorphous material in the electron micrographs. In Werner's syndrome the amorphous material is granular and so profuse that it obscures the collagen fibrils; in scleroderma the amorphous material present is quite different in appearance and has a fluffy character.

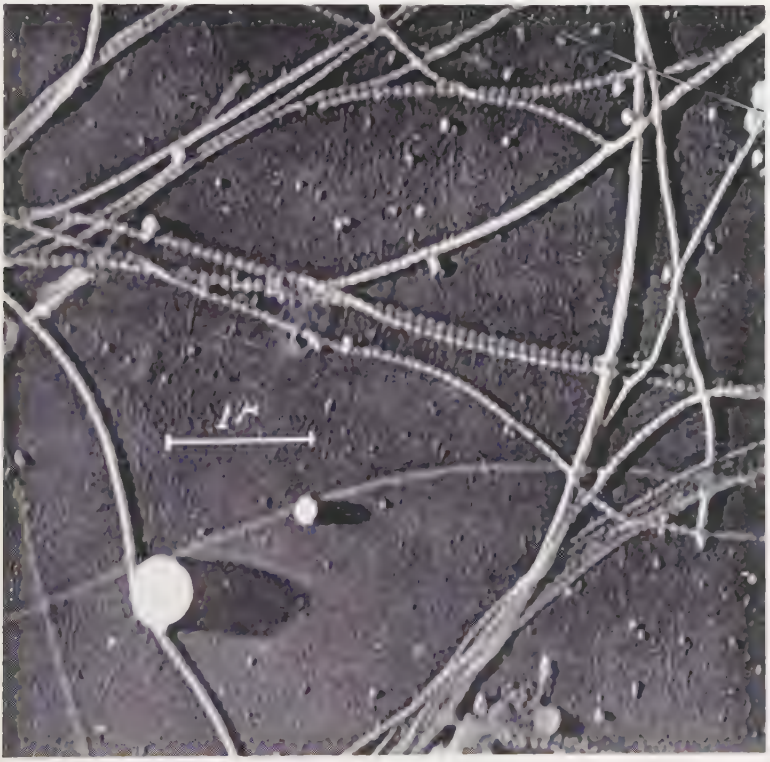

FIG. 5.—The same after digestion with trypsin with much of the amorphous material removed, revealing collagen fibrils. × 13,000.

HISTOLOGY.

In Werner's syndrome the changes are essentially those of atrophy. The stratum spinulosum is thinned and there is flattening and even disappearance of the papillary body. Spongiosis and vesication may be present and the basal layer may show pigmentation. The pilosebaceous apparatus tends to disappear and the sweat glands degenerate. The staining reactions of the collagen and elastic fibres are usually normal, but the fibres may be thin and arranged in bands parallel to the surface. Thannhauser (1945) commented on the poorly developed panniculus adiposus in the affected areas.

While not so marked, alterations of the epidermis in scleroderma of long

standing may be similar, though spongiosis and vesication are rare. The major changes are seen in the dermal connective tissue and smaller vessels: the collagen fibres appear homogenized, sclerotic, and tend to be arranged parallel to the surface; they stain faintly blue with the elastic stain (Lawson or Weigert's), and orange yellow with van Gieson. The elastic fibres are partly obscured by the swollen collagen bundles and there is regression of the subepidermal garland. Proliferation of the intima and narrowing of the smaller vessels may be present as well as minimal perivascular infiltration

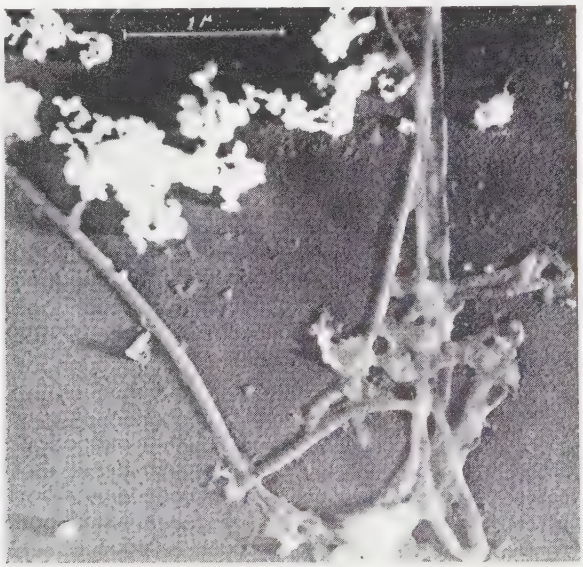

FIG. 6.—Electron micrograph from skin in sclerodermia showing fluffy debris material; a few of the collagen fibrils are bent and shortened. × 14,000.

with small round cells. The pilosebaceous apparatus disappears, though the arrectores pilorum muscles may persist. The sweat glands appear atrophic and are wedged in between the connective-tissue fibres.

COMMENT.

In the case described the skin, hair, eye, vascular, laryngeal, endocrine and degenerative changes as well as the facies and habitus are characteristic. Anidrosis was present and has not been reported previously. The metastatic calcification was out of proportion to the degree of osteoporosis; Herstone and Bower (1944) drew attention to this feature of Werner's syndrome. From the family history it is suggested that *formes frustes* have occurred in the great aunt, father, brother, and possibly sister. As there was no hypertension or other pathological findings it is concluded that the congestive

heart failure was due to degenerative changes in the coronary arteries. Unfortunately it was not possible to have an electrocardiograph until the patient was ambulant.

Dr. D. I. Williams recently allowed one of us (R. H. S.) to examine the case he described in 1949. The similarities between the two patients were remarkable, and they might well have been members of the same family.

FIG. 7.—Electron micrograph from superficial part of a sclerodermatous nodule. There is a little debris material; apart from slight fraying of the ends of a few fibrils, the collagen appears normal. × 13,000.

The presenile appearance of these patients has been attributed to endocrine disturbance and cataracts have been described as being of "endocrine type" (Louw, 1945; Francheschetti and Maeder, 1949). Thannhauser (1945) thought the endocrine changes were secondary to a "defective germ plasm that manifested its multiple defects at different periods of life".

DISCUSSION.

Werner's syndrome is very rare, and because of superficial similarities has been generally identified with scleroderma, but we believe that the natural

history and clinical features of these maladies enables them clearly to be distinguished.

Thannhauser (1945) was one of the first to make this distinction ; he also gave an account of the histology. Histological section shows only the relatively similar results of what are probably two different disease processes. In Werner's syndrome the diagnosis can be made without microscopic examination, and biopsy should not be lightly undertaken as the wound may take months to heal.

Differential Diagnosis.

In Werner's syndrome the skin and underlying tissue of the limbs are chiefly involved ; and in the rare cases where papillation occurs, it is present as a part of the affected areas. Circumscribed scleroderma (morphoea) can therefore be readily distinguished from it by the localized ivory thickenings and tendency to form bands.

In progressive symmetrical scleroderma (acrosclerosis) Raynaud's phenomenon is often present at the onset, and after a variable period there is progressive hardening of the skin of the fingers. The face becomes mask-like, the lips thin and tightly pursed, and small telangiectatic tufts develop on the cheeks. Similar hardening occurs on the forearms, the neck, the upper parts of the arms and chest, and the lower part of the back and abdomen. The feet and lower limbs are occasionally affected in the same way. Arthralgia is frequently an early symptom. In contrast to Werner's syndrome, scleroderma is not familial and circumscribed hyperkeratoses are not present. Calcification is localized to the skin and subcutaneous tissue ; osteoporosis of the distal phalanges occurs when the fingers are involved. Systemic manifestations are shown in the form of lung fibrosis and peripheral cysts, oesophageal changes, and occasional cardiac involvement. The intima of the smaller blood vessels may show thickening and the muscle coats be replaced by fibrous tissue. Affection of skeletal muscle is variable. Most of the oesophageal symptomatology is due to muscle atrophy of the pharynx and oesophagus ; it is suggested that involvement of the diaphragm may lead to hiatus hernia and oesophageal ulceration.

In symptomatic or pseudoscleroderma, areas of hardening and atrophy occur on the legs in association with varicose dystrophy and ulceration, or where there is a chronic affection of the lymphatics. Similar hardening may occur in acrodermatitis chronica atrophicans with thin scaling wrinkled skin, visible subcutaneous vessels and leg ulceration.

The difference between Werner's and Rothmund's syndromes have been pointed out by Oppenheimer and Kugel (1934), Carleton (1943), Thannhauser (1945), Francheschetti and Maeder (1949). In Rothmund's syndrome cataracts usually develop between two and five years of age ; wasting of the extremities

and dwarfism occur much less frequently than in Werner's syndrome. The most characteristic feature of the syndrome is the skin changes, which start shortly after birth and mainly affect the face and extensor surfaces of the limbs. There is an erythematous network with telangiectasia surrounding areas of depigmentation and fine scaling atrophy. Small areas of pigmentation, telangiectasia and depigmentation are seen in the less affected areas. The similarity of these changes to those occurring in Thomson's syndrome (poikiloderma congenitale) has been indicated by Carleton (1943), Rook and Whimster (1949), and Francheschetti and Maeder (1949).

In poikilodermia atrophicans vascularis (Jacobi) there are telangiectasia, atrophy and red miliary lichenoid papules. Pigmented and depigmented spots are present and the lesions are covered with fine corrugations and scales. The condition has been separated from poikilodermatomyositis (Petges) by Dowling (1938). This disease may present as pink swelling of the eyelids and face; later there is an erythematous telangiectasia with fine scaling, pigmentation and depigmentation, and sclerodermatous change. The erythematous changes, which are not unlike those of subacute lupus erythematosus, may be seen arranged in bands on the backs of the fingers and hands. Symmetrical muscle groups tend to be involved and there is pain and weakness. In advanced cases the limbs, shoulder girdle and glutei are especially affected.

In dystrophia myotonica, cataract, testicular atrophy and canities are associated with wasting of the distal muscles and those of the face, the sternomastoids being particularly affected. Myotonia is present in the muscles of the forearms, legs and tongue. In its inheritance, the condition shows the phenomenon of "anticipation" in successive generations.

Summary.

The features of Werner's syndrome are described, a new case is reported, and the differential diagnosis discussed. The histology of Werner's syndrome and sclerodermia is given, with a preliminary report on the electron microscopic findings.

It is claimed that Werner's syndrome can be distinguished from sclerodermia by comparing their natural histories.

The electron microscopic studies were carried out while Dr. Reed was on the staff of the Department of Biomolecular Structure, Leeds University, and the authors would like to thank Professor W. T. Astbury for the facilities provided. We are indebted to Dr. W. Goldie and the members of his staff, who carried out the pathological investigations and made the histological preparations, and to Mr. J. Hainsworth and Miss S. Fry for the photographs and photomicrographs.

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PSYCHIATRIC OBSERVATIONS ON FACIAL DERMATOSES.*

IDA MACALPINE.

Psychosomatic research is a border territory and the more the psychiatrist understands the dermatologist and vice versa the better. The no-man's-land of psychosomatic illness is, however, in danger of becoming everyman's land. Psychiatry is peculiarly and unfortunately often considered to be nothing more than applying common sense to psychological data. A few critical remarks on the general trend are therefore called for.

This paper is intended to show the value of the psychotherapeutic approach in psychosomatic research, namely the detailed study of the individual patient by a well trained psychiatrist. Response to, and observation during, psychotherapeutic sessions is indispensable for accurate understanding of symptoms and their significance, and is a safeguard against unwarranted generalizations. Where the dermatologist looks with a trained eye, the psychiatrist's task is to listen with a trained ear. For both, response to therapy is a tool of diagnostic value. At the present day there is a tendency to replace minute clinical study of single patients during psychotherapy by attempts at finding common, arbitrarily selected traits of personality in large numbers. But statistics and large numbers are not the royal road to psychiatric insight into a patient's conscious and unconscious mental processes. Barber (1952*a*) only recently stressed that one carefully investigated case may be more fruitful than collections of statistics. It is thereby not meant to dispute the role of statistics in confirming known or suspected facts.

The usual approach to psychosomatic problems by establishing personality patterns and types has lately been rightly criticized from various quarters (Cobb, 1952; Macalpine, 1952; Obermayer, 1952). Without enumerating the many valid objections to this approach, and the unconvincing supporting evidence, it may be stated briefly that its main fault lies in the fact that it suffers both from over-simplification and over-complication. The history of Medicine from time immemorial shows that the approach by types and temperaments has proved unrewarding and inconclusive. Similarly, projective techniques cannot replace direct insight gained during psychotherapy, and only have their place as aids to the psychiatrist as laboratory tests help the dermatologist. By themselves tests can never replace the clinical approach, and used alone are as dangerous and misleading as any scientific short cut.

* Read at the 10th International Congress of Dermatology under the title, "Psychotherapeutic Principles in the Treatment of Cutaneous Disease".

It has elsewhere been pointed out that patients with psychosomatic skin lesions are usually and erroneously labelled "neurotic" and the skin symptom considered as part of a neurotic make-up (MacKenna and Macalpine, 1951). But psychoneurotic symptoms comprise only one type of mental symptom formation. Many reasons can be found to explain the neglect of psychotic factors in psychosomatic research: perhaps the most important is the widespread belief that ambulatory patients by the very fact that they are up and about must be neurotic, the institutionalized patient alone seeming to qualify to be called psychotic. In reality, however, many unrecognized near or latent psychotics who never break out in a frank psychosis are to be found among out-patients in all hospital departments, and indeed in the population at large. That psychosomatic symptoms resemble the psychotic rather than the neurotic in most of their features and clinical course has recently been pointed out (Macalpine, 1952). Indeed, it was shown that psychotic mechanisms play the major part in psychosomatic symptom formation. It is not thereby intended to imply that all psychosomatic patients are therefore of necessity psychotic or prepsychotic. Although a patient may have no other psychotic symptoms, if in fact he appears otherwise "normal", or even if he be a "neurotic" personality, his skin symptom may yet be, and mostly is, the product of a psychotic mechanism.

Owing to the work of Freud psychoneurotic symptom formation is much better understood, and this has unduly tinged psychosomatic research and set the fashion of seeing the psychoneurotic in every symptom. It may be thought that the differential diagnosis between psychoneurotic and psychotic mechanisms is of academic interest only. On the contrary, correct diagnosis has far-reaching implications for prognosis, type of and response to psychotherapy. Surprisingly, and contrary to common assumption, psychoneurotic symptoms may be more refractory to psychotherapy than mild psychotic symptoms, and psychotherapy must be based on different principles. Classical psycho-analysis, advocated for the psychoneuroses, is not only contraindicated, but may actually be harmful for psychosomatic patients. This is to be expected in view of the different structure of psychoneurotic and psychotic symptoms. Thus the psychoneurotic symptom is a complicated end-product of a mental defence against instinctual conflict, often expressed symbolically and originating in the sexual sphere. Psychotic symptoms on the other hand are characterized by a breakthrough of unconscious emotions and infantile fantasies. They are not primarily a defence.

For the presentation of this paper are collected a fairly uniform class of patients. They were not selected according to diagnostic labels. Their common feature was a lesion of the skin of the face. Some had been diagnosed as light sensitivity, permanent erythema with burning and itching, angioneurotic oedema of eyes and lips, urticaria, and Besnier's prurigo. Some

patients resembled closely Barber's (1934) description of menopausal lesions of the eyelids. Patients with acne were excluded.

There were 35 patients, of whom 32 were females and 3 males. Their ages ranged from 18-65 years, with a peak between 40 and 50. Duration of symptoms was anywhere between 2 and 12 years.

None of the patients received physical treatment while undergoing psychotherapy, but they were allowed to continue such applications as had been used unsuccessfully before psychotherapy was started. This point is stressed because sometimes psychosomatic illness is described as a condition in which both somatic and psychological treatment ought to run concomitantly. But if this is done evaluation of results is blurred ; further, the patient will not or cannot co-operate wholeheartedly with the psychiatrist while his loyalty is split between the two disciplines. He will, with some justification, take this double approach as a sign that his medical attendants also are far from being convinced of the value of their respective methods, and thus draw continual support for his own attitude, namely to keep at bay such unconscious emotions which find expression but are denied conscious appreciation in the skin symptom.

The majority of patients whom we are at present discussing were free from symptoms after an average of 10 to 20 sessions ; the remainder were greatly improved with the exception of one case with gross lichenification, where in 5 sessions no psychological cause could be detected. More than half of the patients had no recurrence in two years. In patients who relapsed after a free interval the symptom tended to be less severe and could again be cleared in only a few sessions. Whether or not a symptom recurs is of course dependent on many factors, among them the total personality, the degree of environmental stress and the presence of other disturbances. Recurrence of symptoms after psychotherapy should not be used as an argument against their origin being in the psychological sphere. In the same way as an organic lesion may recur despite correct diagnosis and treatment, so can psychosomatic symptoms recur without thereby discrediting the concept of psychological origin or the value of psychological treatment. Psychotherapy should not be likened to a surgical operation removing that part of the mind which causes the symptom ; it rather resembles medical procedures.

The following observations were made :

None of the patients could give a reason for their symptom as it came to be understood in the course of psychotherapy. Many had certain ideas as to the cause ; but in every case this later turned out to be merely a " cover cause " (MacKenna and Macalpine, 1951). For instance one patient attributed her urticaria to eating fish ; attacks occurred every Friday and did not stop when she changed her diet. In the course of psychotherapy it became clear that the outbreaks were related to feelings for her son, who had been killed on

a Friday during the war. Four cases previously diagnosed as light sensitivity, and always worse in the spring and summer, could be traced to anniversaries falling due in those months. Barber (1952*b*) comments on the fact that many such cases are erroneously labelled light sensitivity.

This connection of exacerbation with a significant date is outside the patient's conscious knowledge, and appears as the result of an "unconscious memory". Direct questioning about events of importance at the same time in previous years yields no information. The relevant facts and dates are often obtained in the first history-taking interview without the patient at the time realizing their significance. They must be remembered and subsequently connected up with the outbreak of the symptom in later years. Exacerbation of symptoms due to anniversaries is rare in psychoneurotic patients but common among psychotics, a fact noted by Bleuler in 1911 (Bleuler, 1950).

Precipitating factors must not be taken at their face value; only when the operation of unconscious mechanisms is taken into account can their true significance be assessed. The all too natural approach to patients with the question "have you any worries?" must of necessity be answered in the negative, because the patient is unaware of feelings relevant to his symptom. Were he aware of them he would have no need for it. It is the therapist's task to detect this emotion or unconscious fantasy, trace it to early life situations, understand how it was revived to activity in the present, and work this through with the patient.

Some lesions of the eyelids, first described by Barber (1934), were in our series due to "retained tears". Patients did not, or could not show their feelings of grief at the time of loss, and after a varying interval or "incubation" period developed itchy eyes with scaly skin. After recognizing this connection and being given a chance to discuss and so discharge their pent-up feelings, the skin lesions cleared up.

Frequently among these patients the emotion responsible for the lesion was suppressed anger. In some cases patients had had difficulties with superiors at work whose attitude they resented. It led to symptom formation because it repeated in current life, and so overcharged, a childhood situation towards an educator. Patients seemed "sensitized" to specific situations. As the patient was no longer aware of the emotion, it persisted through lack of adequate discharge, and found vicarious expression in the symptom.

There was in nearly all patients a direct relation to depression. Patients claimed that their disfiguring skin lesion was enough reason to make them feel downcast; but it became evident during psychotherapy that their feeling depressed had often preceded the facial lesion, and there was a tendency for it not to diminish parallel with improvement in the skin.

The appreciation of this depressive element or potentiality in the symptomatology of these patients throws some light on the high incidence in meno-

pausal women : the predisposition of this age group to depression is a well-established fact.

If it is remembered that anger was found to be the emotion expressed in these facial lesions, the connection with depression becomes evident. Depression is not a simple feeling tone, but a complicated, fused affective state, in which anger, anxiety and guilt are blended. In depression anger is no longer directed against the outer world, but is turned against the self, which is felt to be worthless and good for nothing. In the cases under consideration there seems to be a " de-fusion " of the compound affect of depression, and the anger part finds an outlet in the skin lesion. This was particularly striking in cases of " light sensitivity " and " contact dermatitis", in which the face was lobster red, the skin dry, scaly and burning ; the full routine of allergic investigation had not revealed an allergen.

It is important for the psychotherapist to understand this connecting link with a true depression. If these patients are injudiciously managed, a severe depressive state may ensue despite the facial lesion clearing up, or more correctly because of it : the anger, being no longer partly discharged through the symptom, will be turned against the self in all its strength and so precipitate a severe depression. In support of the mechanism here described we may mention three female patients not included in this series, in two of whom the facial lesions resolved spontaneously on the development of a true depressive psychosis requiring mental hospitalization. The third patient while in a mental hospital and recovering from a psychotic episode developed transient lesions of the face and ears. In two further cases again not included in our series the rapid removal of the skin lesion, in one by hypnosis and in the other by drug abreaction, resulted in the development of a depressive psychosis. It follows that the therapist has to be on his guard against this possibility. He will gain respect for the facial lesion, and not treat it as a foreign body to be removed as quickly as possible. He will appreciate the function of the psychosomatic symptom as a means, however inadequate, of maintaining equilibrium in the psychic economy.

One more observation : all patients with psychosomatic facial lesions developed paranoid trends in varying degrees : they became self conscious, avoided being among people, were concerned about their looks and the impression they made on others. Frequently they felt they were being watched, even shunned and suspected of being unclean or contagious. This attitude is in striking contrast to that of patients suffering from organic lesions in the same region. It is found so regularly as to be almost pathognomonic of a psychosomatic origin.

On the negative side, there was an insufficient number of common traits among the patients in our series to allow the establishment of common personality types. Nor was it possible to say that patients showed over-aggres-

siveness, over-dependency, a special tendency to exhibitionism, or guilt. Some showed hysterical, some obsessional traits, some were over-sensitive, some prepsychotic, and many "normal".

Summary.

(1) Psychiatric experiences in the course of investigation by psychotherapy of 35 patients with facial dermatoses of various kinds are described.

(2) The importance of unconscious factors and the similarity between the formation of psychosomatic and psychotic symptoms is stressed.

(3) Anger was the common underlying emotion.

(4) In all patients there was a direct relation to depression. Injudicious management may remove symptoms but precipitate a true depression.

(5) The symptom may be assessed as a masked depression.

(6) Paranoid attitudes about the facial lesion are regarded as pathognomonic of psychosomatic as opposed to organic lesions.

(7) Specific personality types could not be found.

The work described was carried out in the Dermatological Department, St. Bartholomew's Hospital, with the help and encouragement of Dr. R. M. B. MacKenna, Physician in Charge, to whom I wish to express my gratitude. Dr. Richard A. Hunter was responsible for finding the mental hospital cases.

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NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

Liverpool, 14 October, 1952.

Morphoea.—Dr. W. E. Bowden for Dr. F. Glyn Hughes.

A girl aged 13.

History.—Thickening of the skin developed over the inner aspect of the left thigh in March 1951. Similar patches of thickened skin later appeared on the left side of the chest and a gradual extension of the process took place until by October 1951 the skin of the left side of the abdomen, left thigh, buttock, leg and foot was involved. She was at that time referred to an orthopaedic surgeon because of flexion deformity of the left hip and knee.

On examination.—An underweight and under-developed girl. Two isolated patches of sclerodermia are present on the left side of the chest. Other areas of sclerodermia are seen around the left loin, in the left groin, left thigh and on the left buttock. The entire circumference of the left leg, foot and toes is involved in the sclerodermatous process, causing flexion deformity of the left hip and knee.

Marked wasting of the left leg is present and the skin is adherent to the underlying tissues.

There are early lesions on the right thigh and calf.

Progress.—She has been treated with vitamin A, 150,000 units daily by mouth, inunction of a lanolin cream and massage. New lesions continue to appear.

Discussion.—Similar cases were mentioned by Dr. J. H. Twiston Davies, Dr. F. Glyn Hughes, Dr. I. B. Sneddon and Dr. F. F. Hellier in which recovery had occurred after many years. The importance of not allowing early orthopaedic interference was stressed by the speakers.

Case for Diagnosis ? telangiectasia macularis eruptiva perstans.—Dr. Godfrey Bamber.

A women aged 23, was seen first on 2 October 1952 on account of a rash which had appeared a year earlier as red spots on the back and had spread to the arms and legs. It did not itch, and had been unaffected by pregnancy and parturition. Her general health was good and she had not taken drugs of any kind before the onset of the rash.

On examination.—From the neck to the knees are numerous brownish-red macules, some of which show purpura on diascopy. The lesions do not urticate after rubbing.

Blood count : Hb 90%. R.B.C. normal. W.B.C. normal.

Histology. There is intercellular oedema and lymphocyte infiltration of the epidermis. The dermis is markedly oedematous and hyaline without infiltration. Mast cells have been seen but are not present in excess. The appearances point to an urticarial lesion without vesiculation.

Comment.—On clinical and histological grounds angioma serpigiosum and Majocchi's disease can be excluded. The lesions could be classified under Brocq's telangiectasies essentielles en plaques, and may be an unusual form of telangiectasia macularis eruptiva perstans.

NOTICE.

British Association of Dermatology
Annual Meeting, 1953.

The next Annual Meeting of the British Association of Dermatology is to be held in London on 25, 26 and 27 June. The programme provisionally arranged is as follows:

25 June. Morning: Annual General Meeting. Papers on "The Skin Manifestations of Peripheral Vascular Disease."
Afternoon: Short papers.

26 June. Morning: Papers on "Rosacea, with Special Reference to its Ocular Manifestations."
Afternoon: Free.

27 June. Morning: Short papers.
Afternoon: Demonstration of clinical cases.

Most of the meetings will be held at the Royal Society of Medicine.

CORRESPONDENCE

To the Editor of 'The British Journal of Dermatology.'

Sir,—Dr. Lazar and I have noted the recent letter of Dr. H. G. Adamson (p. 345) in which he calls attention to the similarity of our case recently reported in this Journal (**64**, 97, March 1952) to his report on "A Case of Multiple Ulcerating Basal-Cell Epithelioma with Zoniform Distribution and Possibly of Sweat-Gland Origin" which appeared in the *British Journal of Dermatology and Syphilis* in 1917 (**29**, 81).

We wish to apologize for failing to note Doctor Adamson's contribution, and for therefore not giving him due credit. It must be granted that the zonal arrangement of the lesions is common to both of our cases; and there is also the possibility that the lesions may be histopathologically similar.

We asked Dr. Charles F. Sims, who originally studied our sections, to review the findings in the two cases in question. We quote from Dr. Sims's report: "Dr. Adamson's case differs from that of Doctors Witten and Lazar in the following particulars: Dr. Adamson's case reveals masses of basal cells most prominent in the mid- and deep corium and presumed to arise from the sweat glands. The case of Doctors Witten and Lazar presents multiple foci consisting of buds of basal cells arising at different points along the basal cell layer (termed by Jadassohn "multicentric basal cell epithelioma") —a much more superficial process than that observed in Dr. Adamson's case. . . ."

We are, Sir, yours truly,

Victor H. Witten, M.D.
M. Paul Lazar, M.D.

New York.

BOOK REVIEW.

ERICH HOFFMANN.*

This autobiography bears the subtitle " Memoirs from a Turning point in Medicine." Apart from the individual and medical interest, it gives a panorama of cultural, political and historical development during the period before the first world war to the present time.

The first volume, called " Endeavour and Creation," gives a detailed account of the author's background, his youth, studies and gradual rise to fame in the medical world. All this is accompanied by numerous philosophical, political and psychological contemplations, viewing life and world from a higher angle. The chapters dealing with the discovery of *Spirochaeta pallida* in association with Schaudinn, their struggle at first for certainty and then for general recognition, make truly dramatic reading. Other significant parts of the book deal with the author's pioneer work in early antiluetic treatment, his studies on Atoxyl, an organic arsenical compound and forerunner of Ehrlich's great discovery, his efforts for the recognition of dermatology as an equal among other specialties, and for an aetiological classification of dermatoses as an advance over the hitherto purely morphological systems—these are a few highlights out of the imposing wealth of ideas, investigations, papers, congress contributions and debates filling the pages of this book, the second volume of which bears the significant name, " Struggle for perfection."

The author's interests extend far beyond the purely medical field. He is a great traveller and has seen most of the globe, giving vivid accounts of his impressions. All the arts fill him with ardent admiration and he is no mean poet himself, giving numerous examples of this facet of his creative talent.

Where world history and the personal life of Professor Hoffmann become closely entangled the book is a document of personal heroism. His open and unswerving opposition to the Nazi regime makes him one of its self-chosen victims—he loses his Professorship at the Bonn Clinic, the development of which he counts among his proudest achievements.

The closing chapters deal with the horrors of the aftermath of World War II, but the book ends on a hopeful note, expressing Professor Hoffmann's unshaken faith in mankind's eventual rise to peaceful happiness.

G. H. R.

* *Lebenserinnerungen aus einer Wendezeit der Heilkunde.* By ERICH HOFFMANN. Hanover : Schmorl & Von Seefeld Nachf., 1948 and 1949. 2 volumes. Pp. 403 and 309. 3 illus.

CURRENT LITERATURE.

THE INFLUENCE OF CHOLESTEROL FEEDING ON THE FAT OF THE SKIN SURFACE IN THE RABBIT. H. Lincke. (1952) *Dermatologica*, **104**, 71.

Thiouracil alone had no effect on the cholesterol content of rabbit sebum, but with the addition of cholesterol to the diet an increase was noted. With 100 mg. daily of thiouracil the cholesterol-cholesterol ester ratio in the sebum was unchanged, but with 200 mg. daily the increase in the sebum was due almost entirely to pure cholesterol. Although in these animals the cholesterol in the blood rose to ten or even twenty times normal, the cholesterol-cholesterol ester ratio was unaltered. J. F. S.

TREATMENT OF PSORIASIS WITH VITAMIN A, WITH A NOTE ON HYPERVITAMINOSIS A. J. R. Frey and M. A. Schoch. (1952) *Dermatologica*, **104**, 80.

Nine cases of psoriasis were treated with vitamin A, 400,000 i.u. daily, for from one to three months. Two became clear; seven were unimproved. Dryness of the lips occurred in most, and the administration of very large doses, 1,000,000 to 4,000,000 i.u. daily, to two of these patients produced diffuse redness and scaling of the non-psoriatic skin, depapillation of the tongue, nausea and dizziness. J. F. S.

STROPHULUS AS AN INFECTIVE DISEASE. A. A. Botter. (1952) *Dermatologica*, **104**, 87.

After a long discussion of the clinical features of strophulus, and theories as to its cause (but, curiously, without once mentioning possible psychological factors), Botter describes experiments in which he produced a papular rash, resembling but not identical with strophulus, in 8 children whose strophulus had disappeared spontaneously with hospitalization, and 1 child with eczema, by intranasal instillation of ultra-filtrates of washings from the pharynges of four mothers of strophulus children. In a total of 22 such inoculations he had no failures. He could not demonstrate a virus in the filtrates. J. F. S.

AN ATTEMPT AT THE CLASSIFICATION OF THE EOSINOPHILIC GRANULOMAS OF THE SKIN. M. J. Woerdeman and J. R. Prakken. (1952) *Dermatologica*, **105**, 133.

This is a very good attempt to bring order out of something like chaos. From its nature the article does not lend itself to condensation, and it should be read in full by all interested. It is in English. J. F. S.

PITYRIASIS SIMPLEX FACIEI. A. Brand and J. Tas. (1952) *Dermatologica*, **105**, 145.

Brand and Tas investigated the occurrence of "dartre volante" in Israeli school children, and found a significantly higher incidence in poorer children, and in those of darker complexion. General nutrition did not appear to be significant, and bacteriological studies yielded no clue to the cause, but personal cleanliness did seem to be a factor. J. F. S.

MELANOSIS DORSALIS. O. J. Costa. (1952) *Dermatologica*, **105**, 166.

Aguëlles Casals in 1938 and Orol Arias and Pessano in 1939 described a peculiar pigmentary disorder of the interscapular area, which so far has not been noted outside Latin America. Costa reports from Brazil a characteristic case but can throw no clear light on the aetiology. J. F. S.

CHANGE IN OUR NEUROHISTOLOGICAL VIEWS AND THE TREATMENT OF NEURO-VEGETATIVE SKIN DISEASE. F. John. (1952) *Derm. Wschr.*, **126**, 860.

A discussion on the physiology of the neuro-vegetative system and recent changes in opinion. One no longer speaks of a sympathetic-parasympathetic antagonism in the morphological sense. Atropin may restrain the action of acetycholine and ergotamin that of adrenalin, but not vice versa. It is now known that the Langerhans cells of the epidermis are nervous elements, and the internal secretory function of the stalagmocytes is recognized as explaining morphologically the theory of esophylaxis.

He describes the successful treatment with intramuscular pendiomid of three very different types of complaint involving the nervous system. The extreme pain of a haemorrhagic herpes zoster disappeared in three days following 100 mg. of pendiomid given daily for two days. Severe itching of three weeks' duration, thought to be associated with a liver tumour, disappeared with five daily injections, and with five others was still gone two months later. A patient with frequent migraine attacks and paraesthesia of one arm with an occasional dead finger was symptom-free in nine days after four injections. Earlier in his article the author discussed the mode of action of local sedatives applied to the skin, and suggested the participation of the epidermal cells forming part of the peripheral network of the nervous system.

He explains the uniformly satisfactory response in the three patients treated with pendiomid by suggesting that this could be due only to an effect on the conductor substances of the ganglion cells: in the periterminal network of these cells are the synapses (i.e., in the neuro-vegetative syncytium or terminal reticulum)—the real target of attack of such remedies. M. S. S.

CHRONIC DEEP CUTANEOUS ENTEROCOCCAL GRANULOMAS. G. W. Korting. (1952) *Derm. Wschr.*, **126**, 999.

In a man aged 24 deep acne conglobata or scrofuloderma-like lesions in axillary genitocrural and perianal regions with fistula formation gave a pure culture of a streptococcus of the group of enterococci (Serological Group D). There was no gastro-intestinal upset. An intracutaneous test with an autovaccine gave a strong positive reaction (negative in three controls), with slight evening temperature and aggravation of the lesions. The histology was that of a chronic non-specific granuloma with irregular acanthosis and profuse especially perivascular infiltration of round cells and plasma cells mainly. Treatment with oral aureomycin combined with antibiotics locally in watery solution; aureomycin and chloromycetin, to which the organism was sensitive, supronal, etc., was successful. M. S. S.

THE POPOFF TRYPAN BLUE TREATMENT OF DUHRING'S DISEASE. G. W. Korting. (1952) *Derm. Wschr.*, **126**, 1065.

The author discusses the rationale of the relatively little known trypan blue treatment of dermatitis herpetiformis introduced by Popoff 19 years ago. The rarity of spontaneous remissions or remissions of any duration even following treatment lends significance to the high percentage of favourable results (8 out of 14 patients) obtained by this method (sometimes following an exacerbation after the third–fifth injection). Side effects were relatively unimportant.

The author gives a detailed description of the clinical findings and response to treatment in several patients. He thinks the young patient may respond less well than the older. The treatment was unsuccessful in a child aged 4, but a patient aged 80 complaining for one year became clinically healed within 14 days after nine intravenous injections of 0·1 ml. rising to 0·2 ml. of a 1% watery solution. This should be as freshly prepared as possible (it tends to form a sediment on standing for 24 hours), sterilised and injected rapidly into the vein every second day. Usually 1 ml. of a 1% solution is given without increasing the dose (children should have a proportionately smaller dose), but occasionally this dose is too large—has a provocative effect leading to leucodiapedesis—and it is safer to begin with smaller doses as in pyrotherapy, and to increase the interval to 3 days. The author prefers on the whole not to exceed 8–10 injections (Popoff, 30–40). A relapse in 2 out of 8 patients in two years responded again to 3–5 injections. Contraindications to trypan blue therapy are anaemia, with tendency to pulmonary oedema, disturbed R.E.S. function (e.g., post-malarial splenomegaly) or after Germanin as this has an effect on the R.E.S. One patient previously treated with Germanin responded very badly to trypan blue but not so a patient previously treated with sulphonamide. M. S. S.

GENERALIZED MONILIASIS. W. Nikolowski and I. Miller. (1952) *Derm. Wschr.*, **126**, 969.

The findings in 4 patients are described. (1) Female aged 45 with a history of relapsing pyrexia of unknown origin. No improvement with penicillin or terramycin. Agranulocytosis (300 leucocytes) with irgapryin. On admission an eruption was already present in the genitocrural region. This spread during the antibiotic therapy to involve lower trunk, back, neck, buttocks and upper thighs as a mainly follicular or perifollicular discrete eruption. Microscopically: Large clumps of spores with scanty hyphae. On culture *Candida albicans*. Urethral smear and urinary sediment positive. Sputum and blood culture during fever negative. Local fungicidal treatment showed a response only when the leucocyte count rose and iodine calcium was given internally.

A second patient, a diabetic aged 65, with a past history of pneumonia, pleurisy, lung emboli, etc., and suffering from a hemiplegia, thromophlebitis and vulvitis, after 14 days' penicillin therapy developed intertrigo of all the large flexures with macerated scaly border and a discrete eruption pinhead to farthing-size of other areas.

The third patient was a baby with an extensive eruption of the trunk, extremities and scalp : pinhead to palm-sized red lesions (with free fringe 1 cm. broad facing inwards) but no mouth lesions. The generalized eruption followed treatment with a " white salve " of the original lesion of the foot (the mother had mycosis of the arm). Microscopically : slightly branching hyphae with mycelial sporing resembling trichophyton or epidermophyton rather than monilia. Culture negative. The monilia-like appearance of the eruption is probably due to the age of the child.

The fourth patient, a baker aged 35, developed a generalized eruption following treatment with penicillin ointment of intractable fissuring at the angles of the mouth due to monilia. All the interdigital webs of the toes were similarly infected. The generalized eruption resembled a psoriasiform seborrhoeic eczema rather than monilia and the author regards it as due to penicillin sensitivity.

The author draws attention to the importance of general disease and the use of antibiotics in the pathogenesis of generalized epidermal moniliasis. M. S. S.

A STUDY OF TOPICAL THERAPY IN TINEA CAPITIS. M. Sullivan and E. S. Bereston. (1952) *J. invest. Derm.*, **19**, 175.

Chlorosalicylanilide was the best of the 13—many of them having just as long names—evaluated. J. H. T. D.

URTICARIA PIGMENTOSA ASSOCIATED WITH BONE LESIONS. S. G. Clyman and C. R. Rein. (1952) *J. invest. Derm.*, **19**, 179.

Three cases, one already described (*J. invest. Derm.*, **18**, 425), and the x-ray appearance of the lesion different in each—cystic osteoporosis of rib, calcified infarcts of marrow, multiple hereditary osteochondroma. No bone biopsy yet. Discussion ranging from skiagraphic invisibility of known mast-cell accumulations to the absence of bone changes in cases presenting nodular lesions in the skin. J. H. T. D.

USE OF A QUARTZ FIBER MICROBALANCE FOR HISTOCHEMICAL INVESTIGATION OF SKIN. K. Schmidt-Nielsen and E. Taylor. (1952) *J. invest. Derm.*, **19**, 157.

There is nothing very spectacular about the histochemical investigations themselves, which were apparently only intended to demonstrate the reliability of the method. Alternate 10μ tangential sections of a 5 mm. punch biopsy were mounted or alternatively analyzed to show the water lipoid, etc., content of the skin at various levels. Weighing had therefore to be accurate to 0·1 mg. The spring of any balance suitable for the purpose must be of quartz, because that material has the unique property of perfect elasticity, with the limit thereof coinciding exactly with the breaking point.

The little weighing machine looks as if it could quite easily be home-made. J. H. T. D.

THE PATHOGENESIS AND HORMONAL RESPONSE OF ACROCALCINOSIS. F. Fleck. (1952) *Derm. Wschr.*, **126**, 993.

Calcium deposits never take place in healthy tissue, but arise from quite a complex of aetiological factors, local and other. The author cites many instances of hormonal dysfunction and calcinosis. During pregnancy there is a risk on the other hand of hypocalcinosis.

He describes the benefit from ovarian injections in a woman aged 57 with acrocalcinosis in the region of some of the larger joints as well as of the fingers ; slightly raised serum calcium of 11·2 mg. %, and senile atrophic genitalia (menopause 9 years previously). Depot-Ostromon (12 mg.) was used to approximate as far as possible to a physiological dosage over a prolonged period. The contained biologically inactive dimethylether of diethylstilboestrol is gradually converted to the active diethylstilboestrol. After a second dose in 8 days the patient announced spontaneously that the fingers were softer. Improvement continued, but after the fourth weekly injection oral progynon C was substituted as there was complaint of headache, wild dreams and unrest. Up to date ethynol oestradiol suffices to continue improving the calcinosis and to prevent fresh deposits, but it is possible that cessation of treatment may lead to recurrence.

M. S. S.

AMYLOIDOSIS. H. Sprafke. (1952) *Derm. Wschr.*, **126**, 1017.

Out of 146 biopsies on very diverse dermatoses and tumours of the skin, with no regard to localization of the lesion or age of the patient, the author found evidence of amyloid in 4, demonstrated best with congo red. In no case was it possible on biopsy to demonstrate amyloid stained *in vivo* by the local injection of a 0·1–0·5% solution. The four amyloid-containing lesions were granuloma annulare, urticaria pigmentosa, osteoma and naevofibroma, and the amyloid was found as a dense narrow zone in the corium under the epidermis, but not involving the papillae; vessels were not involved. No giant cells or crystals were present. The amyloid lay reactionless in the tissue and lymph spaces and also in areas of sound skin. No patient was older than 35, and the youngest was 19. The author wonders if the presence of amyloid stimulates tumour formation as the findings of Freudenthal in keratosis senilis would suggest (16 positive out of 50 biopsies). The author himself found no amyloid in 7 cases of keratoma senile, and suggests as a reason that they had not been examined at the right stage of development; in one the lesion was calcified. M. S. S.

THE AETIOLOGY OF ACRODERMATITIS CHRONICA ATROPHICANS. T. Grüneberg. (1952) *Derm. Wschr.*, **126**, 1041.

The author favours a spirochaetal genesis for this disease. In support of his view is the frequency of a positive pallida reaction (7 of his own patients had all a positive reaction, 5 of them + + + +, while 8 patients with circumscribed scleroderma tested at the same time were all negative; 3 of 12 patients with acrocyanosis and 1 of 8 with frost bite gave a weak positive). The dramatic effect of penicillin therapy (even better than combined salvarsan and bismuth) supports his view, and the histology also supports an infectious aetiology; the well-marked predominantly perivascular infiltration of lymphocytes, spindle cells, and in the early stages the abundant masses of mast cells; important vessel changes with thickening of the vessel wall and sometimes narrowing and even thrombosis. The E.S.R. is often high (in 15 of 21 patients treated recently it was 43–82 mm.), and in the blood picture there is a slight shift to the left.

The author considers that the positive pallida reaction results from a group reaction to spirochaetes, since Plaut-Vincent's angina and other similar diseases give a similar strong reaction. Predisposing factors in the aetiology of acrodermatitis chronica atrophicans are probably hormonal factors, since it occurs predominantly in women, neurovegetative disturbance, cold and traumatic injury and also an inherited weakness of elastin. M. S. S.

INVESTIGATIONS INTO THE ORIGIN OF INCLUSION MATERIAL OF L.E. (HARGRAVES-HASERICK) CELLS. W. Hauser. (1952) *Derm. Wschr.*, **126**, 1161.

Phagocytosed material of L.E. cells may arise not only from adult segmented neutrophil polymorphs, but from very varied sources, e.g., myelocytes, eosinophils, basophils and also reticulum cells; also experimentally with L.E. plasma from lymphocytes (more marked following freezing) from the blood of a patient with lymphatic leukaemia (not all workers equally successful); also from leucocytes containing phagocytosed red cells from a patient with myeloid leukaemia, but from other blood rich in leucocytes no result. The author found that with prolonged standing of heparinized peripheral blood of an L.E. patient 90% of the leucocytes were transformed into L.E. cells (against a participation of the lymphocytes), and lymphocytes from lymphocyte-rich tissue fluid from skin areas of a patient with lymphadenosis benigna cutis gave a very successful result. The author includes among others several photographs of leucocyte rosettes round a heap of platelets from the blood of an acute L.E. patient during a remission and following ACTH, but while the peripheral blood was not entirely free from L.E. cells. Another photograph shows granular inclusion material staining deeply blue within a leucocyte-rosette, and still a further shows platelet rosette with similar granular material—probably arising from degenerated platelets. M. S. S.

INFLUENCE OF PERCUTANEOUS HEPARIN RESORPTION. G. Stüttgen and H. Weidenbach. (1952) *Derm. Wschr.*, **126**, 1164.

A series of comparative experiments were carried out to test the effect of heparin absorption through the skin. First an extensive area of the skin of the back was vigorously brushed to produce a lively reaction. The coagulation time of the blood plasma was tested before and after the experiment; and after it was found to be reduced -a histamine effect. Nicotinic acid ester (Rubriment or Trafuril) 2·5%, known to have a rubifacient effect, was combined with heparin 5000 units in 10 g. of a eucerine base (Thrombophob salve) and massaged into the skin of the lower

legs for 4 minutes. Prolongation of coagulation time resulted, and the result was greater and more rapid than with heparin alone in the salve ; the effect was still noticeable 1–3 hours later. The heparin nicotinic acid ester salve astonishingly had more effect on coagulation time than the same dose of heparin given intravenously. Nicotinic acid in a salve had an inconstant action on coagulation time. Rise in local temperature following the rubifacient effect of nicotinic acid ester salve (1°-3°) is less than that following vascular dilatation due to the blocking effect of sympathine, etc., but is very definite, particularly in areas with poor circulation. The rubifacient effect of nicotinic acid ester combined with the absorption of heparin in Thrombophob salve should prove useful in the local treatment of thrombosis and phlebitis and a definite dosage can be given. The technique of the experiments is described in detail. M. S. S.

POROKERATOSIS MIBELLI WITH INVOLVEMENT OF THE CORNEA. W. Kiessling. (1952) *Derm. Wschr.*, **126**, 1168.

A child aged 11 who had suffered from porokeratosis Mibelli of the outer side of the left lower eyelid since the age of 1 year had conjunctivitis and garland-like porokeratosis (almost certainly) of the cornea scarcely visible to the naked eye, and astonishingly like porokeratosis Mibelli of the skin, staining with fluorescin. The original skin lesions were treated successfully with thorium X, but the extension on to the lid margin could not be treated so successfully owing to constant lacrymation. Finally with excision of this portion the conjunctivitis cleared up. M. S. S.

THE PATHOGENESIS OF ALOPECIA AREATA AND VITILIGO. G. Màramarosi and E. Nagy. (1952) *Derm. Wschr.*, **126**, 1185.

With the capillary microscope it is possible to observe the behaviour of the capillaries and of the plexus in the sub-papillary layer over an alopecia or vitiligo patch and to draw conclusions as to the vegetative tone of the area. In the authors' experiment intracutaneous histamine and acetylcholine and intravenous sympathicolytics were used—0·1 c.c. of the lowest concentration which would give rise to dilatation in the injected area. In alopecia areata histamine had little if any influence on the capillaries and none on the sub-papillary plexus. Acetylcholine on the other hand caused dilatation of the sub-papillary plexus causing live redness, and after 5 minutes 15–16 dilated capillary loops appeared, but dilatation of the capillary loops did not reach the same degree as on other areas of the body surface showing dilatation. On other areas of the body surface the behaviour to histamine and acetylcholine was different. After histamine there appeared a rapid increase in the number of capillary loops and in their dilatation ; after acetylcholine the reaction was always weaker. This explains why other investigations have failed to show a general sympathicotonia, and in keeping with this failure the author found sugar tolerance curves to be generally normal. Over vitiligo patches only a few pale capillaries here and there could be seen, but over the hyperpigmented border the capillaries were normal. The capillaries of the intact skin in vitiligo (as in alopecia) following histamine showed much more dilatation, and were much greater in number when compared with the depigmented areas. Acetylcholine gave a weaker reaction than histamine, and adrenaline caused no apparent reaction. Examination with the capillary microscope 1 hour after 3 c.c. of intravenous tetraethyammonium bromide yielded a result comparable to that after local acetylcholine. Thus in vitiligo and also in alopecia sympathicotonia is local not general. In two of the authors' patients with alopecia and vitiligo loss of pigment preceded the loss of hair. M. S. S.

THE TREATMENT OF PSORIASIS ARTHROPATHICA WITH IRGAPYRIN AND BUTAZOLIDIN. H. Ulbricht. (1952) *Derm. Wschr.*, **126**, 1189.

The author has been unsuccessful in an eighteen months' experience of treating psoriasis arthropathica with adrenal cortex or ACTH. Treatment with irgapyrin (Geigy, Basle) proved much more successful in six patients given each of the treatments in turn. Irgapyrin led to the disappearance of joint pains in every patient, the remission lasting for over six months in 3, over two weeks in 1, and during the period of administration in 2. ACTH and eucortone had each an effect lasting more than 14 days in only 1 patient. Butazolidin was found in all patients to have an action similar to irgapyrin. An abscess at the site of an irgapyrin injection developed in 1 patient, and in 1 instance with irgapyrin and with butazolidin a fall in leucocytes to 3500 resulted, rising on cessation of treatment. Irgapyrin caused a temporary aggravation of a pustular psoriasis but could be continued after a 2 days' rest. After treatment with irgapyrin improvement in the skin appearance was seen as frequently as aggravation. M. S. S.

SEROUS INFLAMMATION AND CORTISONE IN SKIN DISEASES. H. Kutzim. (1952) *Derm. Wschr.*, **126**, 1192.

The author compared the contents of a cantharides blister and the blood serum in a variety of patients ; a quantitative estimation of the protein and NaCl, and a qualitative estimation by paper electrophoresis. He found quantitative difference between the bulla content and blood serum, but the investigation showed evidence of variation in capillary permeability for protein in the different diseases. Eppinger gives as normal an average difference of 2·24, and in patients with heightened capillary permeability a difference of 1·16. In a group of six diseases in the author's experiment the difference was less than 1·16. This group included chronic L.E., pemphigus vulgaris, dermatitis, eczema, purpura and urticaria. On the other hand, in a group consisting of psoriasis, alopecia, condylomata acuminata, pyodermia and ulcus cruris the difference was invariably higher than 1·6. The diseases in the former group consists of patients with " serous inflammation "—diseases as it happens which respond to cortisone and ACTH ; these apparently exert a restraining action on " serous inflammation." Further investigation must prove whether cortisone remedies the heightened capillary permeability or acts on some other factors.

M. S. S.

THE DIAGNOSTIC USE OF VARIOUS FUNCTION TESTS OF THE PERIPHERAL BLOOD-VESSELS IN CERTAIN DERMATOLOGICAL CONDITIONS. W. Blaich and U. Gerlach. (1952) *Derm. Wschr.*, **126**, 1046.

The author compared the efficacy of three tests in investigating the functional activity of the peripheral blood vessels in 60 individuals. 14 had dermatopathia cruris, e.g., ulcers, acrodermatitis atrophicans, scleroderma, etc. Healthy young men and women were used as controls. Cold and hot water (300 c.c.) were given to drink, and the temperature of the skin of the hands and feet was taken before and after. The finding in skin patients and controls was much the same. In the standing test (standing for 15 minutes after lying for 45 minutes) the temperature was taken before and after standing. Patients reacted very much like the controls, except that the skin temperature of the feet after standing rose more than in the controls. With hypersystolic constriction of the extremities with a blood-pressure band for 10 minutes almost no patient showed normal behaviour of the feet as compared with the controls (for the most part there was either no reactive hyperaemia, or a fall in temperature, but a rise could be obtained with priscol). The hands behaved similarly in both patients and controls. While the third test is more likely than the other two to show departure from the normal in the functional activity of the peripheral blood vessels, it should be combined with other functional tests. M. S. S.

FORMS AND INDICATIONS FOR FOAM RUBBER AND BANDAGES COMBINED WITH FOAM RUBBER. R. Brett. (1952) *Derm Wschr.*, **126**, 1116.

In the treatment of a leg ulcer the aim of a bandage should be to tone the tissues and help the circulation or to correct and fix. A zinc gelatine bandage is a rigid bandage which corrects and fixes but has no tonic effect, while the purely elastic bandage becomes readily loosened, having thus only a short-lived effect; it requires to be changed daily to utilize the tonic effect of the muscles and thus help the circulation in vessels and lymphatics. Foam rubber bandages do not serve this purpose effectively and have certain disadvantages ; they are heating, more expensive, and can obstruct the circulation. The author suggests a combination of an elastic bandage and a stiff surface layer of mull or strong gauze for a fixing effect (a " plastic " bandage) ; this allows the ulcer to be cared for and is cheaper than foam rubber, but can be combined if desired with a pad of foam rubber over the affected area : or foam rubber can be applied as a layer flapped round the limb over an elastic bandage (over a zinc gelatine bandage it would be too heating). M. S. S.

THE DEMARCATION OF LYMPHADENOSIS NON-FOLLICULARIS BENIGNA CUTIS FROM SKIN MANIFESTATIONS OF CHRONIC LYMPHADENOSIS. K. W. Kalkoff. (1952) *Derm. Wschr.*, **126**, 1146.

Only histological examination and the finding of germ centres or a predominantly monomorphous lymphoreticular dermal infiltrate allows one to distinguish a lymphadenosis follicularis benigna cutis or lymphadenosis non-follicularis benigna cutis from a later development of a lymphoreticular infiltrate into a leukaemic form from a mobilization of lymphocytes into the blood from the skin or from a subsequent development into a generalized lymphadenosis ; from a lymphoreticular hyperplasia of the skin as an associated manifestation of an aleukaemic or

leukaemic lymphadenosis ; or from a lymphocytic infiltrate of the skin coincident with an aleukaemic or leukaemic lymphadenosis. The author describes two patients with skin infiltrates borderline between the prognostically benign lymphadenosis non-follicularis benigna cutis and skin manifestations of a chronic lymphadenosis. The symmetrical pruriginous papular eruption on face and arms in the first was quite in keeping with a chronic lymphadenosis, but the predominantly lymphocytic character of the lymphoreticular (but not monomorphous) infiltrate together with the negative findings on a general examination (including sternal puncture) allowed a diagnosis lymphadenosis non-follicularis benigna cutis. This was the diagnosis in the second patient, who had symmetrical rubbery sarcoid-like atrophic lesions of cheeks and nose (with reticular network of dilated vessels) and arms with red prominence of the follicles (yellow on diascopy) and lowering of skin temperature over the lesions, also a predominance of lymphocytes in the lymphoreticular exudate. M. S. S.

COAL TAR TREATMENT IN DERMATOLOGY (WITH PARTICULAR REFERENCE TO THE TAR PREPARATION " RODLEBEN "). H. Flegel. (1952) *Derm. Wschr.*, **126**, 1233.

Tar is usually employed when the acute phase of dermatitis has passed. A 40% coal tar preparation in a neutral paraffin wax base was prepared for the author by Rodleben after experiment, and has now been used in 2000 patients, usually where mild tar treatment is indicated but not yet pure tar. Subacute and chronic eczema and lichen simplex chronicus respond well, and it may be followed by pure tar in inveterate eczema. Eczema in children and particularly fissured eczema behind the ears does well, but not secondarily infected eczema. After smears the part should be powdered and covered with a light gauze dressing. M. S. S.

RETROBULBAR CHANGES IN THE TREATMENT OF TUBERCULOUS SKIN AFFECTIONS WITH HIGH DOSES OF VITAMIN D_2. K. Wulf and K. Ullerich. (1952) *Derm. Wschr.*, **126**, 1235.

The authors were unable to repeat the findings of F. Diener in the treatment of cutaneous tuberculosis that retinal haemorrhages accompanied symptoms and signs (e.g., slightly raised serum calcium, haematuria and albuminuria) of intolerance following high doses of vitamin D_2, and that this could be used as a test for early intolerance. They gave 50 lupus patients a similar or higher dose of vigantol-forte (15–96 c.mm.), and encountered signs of intolerance in 3 patients but no ocular changes. M. S. S.

THE AETIOLOGY OF PITYRIASIS SICCA FACIEI. W. Schmidt. (1952) *Derm. Wschr.*, **126**, 1128.

The author finds this a most refractory condition to treat and prefers locally ichthyol soap and 1% ichthyol zinc bismuth salve. Two of his own children he found to clear spontaneously following adenotomy. Since then he has had his patients examined by the rhinolaryngologist, and in all there was found either hypertrophic tonsils or chronically inflamed adenoids. Of these, 7 children were operated on and the skin eruption cleared within several months without local treatment in all but one whose skin condition relapsed after adenotomy ; the parents of this child would not permit tonsillectomy in spite of a history of sore throats. The author considers that focal sepsis is an aetiological factor in this complaint. M. S. S.

ERYTHEMATODES IN HOMOLOGOUS TWINS. H. von Grünhagen. (1952) *Derm. Wschr.*, **126**, 1089.

The occurrence simultaneously in the same year of erythematodes of the face in homologous twins is described (with photographs) and the literature is reviewed. Only once has the author found it described in twins, although as a familial occurrence it is not so rare. Both gave a history of rheumatism and had carious teeth. One had had the tonsils removed on account of sore throats. The other developed a patch of L.E. on the scalp following a burn at the hairdresser's four years before the face involvement. M. S. S.

THE PATHOGENESIS OF MULTIPLE NEUROTIC SKIN GANGRENE. H. Langhof. (1952) *Derm. Wschr.*, **126**, 976.

A woman aged 73 in the third week of an attack of influenza accompanied by high fever developed suddenly overnight with severe pain multiple haemorrhagic infarcts involving the greater part of the skin of face and arms. Two weeks before the onset of the influenza urticarial wheals had appeared over the now affected areas but subsided without treatment in a day. When

apyrexial the erythrocyte count was 2·92 million and the haemoglobin 63%. Bilirubin (indirect) was increased in the serum ; the urine contained coproporphyrin ++, and bile temporarily. The spleen was palpable. Reticulocytes rose from 6‰ to 70‰, and fluorecytes were 20‰, indicating raised blood porphyrin. Severe constipation with indicanuria accompanied the porphyrinuria, and later oliguria with albuminuria, red cells and cylindruria developed. There was evidence of liver damage in a positive Takata. With vitamin B complex and lactoflavin the urine became clear and the skin healed with hypertrophic scars within two months. The histology showed vessel wall damage and perivascular inflammation with narrowing of the vessels. No periarteritis nodosa. Necrosis of the skin.

In the author's opinion the general symptoms could be related to a large extent to the prophyrin ; such a relationship has been described previously accompanied also by neuralgia and symmetrical neuritis, with excitation of the diencephalon vasomotor centres. Women in particular with a neuropathic constitution may suffer from porphyria, and this is the type in whom multiple skin gangrene is found. M. S. S.

DEMONSTRATION OF AMINO ACIDS IN THE SWEAT BY PAPER CHROMATOGRAPHY. H. Wohnlich. (1952) *Derm. Wschr.*, **126**, 945.

The author has demonstrated many amino acids in normal sweat by paper chromatography, apparently the first time this has been done, although Hier, Cornbleet and Bergheim demonstrated 10 by microbiological methods, and Korting and Nitz-Lutzow have used paper chromatography in investigating the amino-acid content of skin dialysate. To the number of amino acids already demonstrated the author has added serine, glycine, alanine, aspartic acid and glutamic acid, and in psoriasis and to a less extent seborrhoeic eczema, cystine. He demonstrated in sweat also the precursor of dopa—of particular interest because previously he had succeeded in demonstrating dopa oxidase in darkly discoloured sweat. As histidine is the mother substance of histamine he suggests that a comparison of the histidine content of normal sweat and allergic sweat might throw some light on the problem of sensitization. Photographs illustrate the findings and one shows well the " train " of cystine. The technique is described. M. S. S.

THE EFFECTIVENESS OF BARRIER CREAMS IN THE PREVENTION OF OCCUPATIONAL DERMATOSES. C. Carrié and G. Lotz. (1952) *Derm. Wschr.*, **126**, 855.

The author tests the efficacy of various barrier preparations, against alkalis using increasing strengths of washing soda solution and against acid and lipoid soluble media, using a turpentine substitute tetraline.

Patch tests with alkali or tetraline were applied to the back for 24 hours. The protective test preparations, vaseline, eucerine, lanette wax, etc., were laid on for 10 minutes before the application of the test patch, then carefully wiped off (no such previous application in the control series).

In both series it was found that fat-containing preparations were more protective than others. Against alkali, eucerine and lanette wax were most effective, then vaseline ; they were less effective against tetraline, but of the three eucerine proved better than lanette wax or vaseline, which were of equal value. The pH of all barrier preparations lay between 6·0–6·5—one only was 7·0. Occasionally the barrier preparation heightened the reaction to the test patch. M. S. S.

THE STABILITY OF ALCOHOLIC AUREOMYCIN, PENICILLIN, PICROMYCIN AND TERRAMYCIN SOLUTIONS IN RELATION TO THEIR PRACTICAL USE. K. Wulf. (1952) *Derm. Wschr.*, **126**, 921.

In an ice chest and at room temperature the stability of a solution of 40 units of penicillin or 1 mg. of the other antibiotics in 1 c.c. of 70% alcohol is compared with that of a watery solution of similar strength, the antibiotic activity being tested against the *Staphylococcus aureus haemolyticus*.

In the ice chest penicillin and aureomycin in sterile water maintain average stability (penicillin slightly more so than aureomycin) up to 60 days ; at room temperature the stability is less. In alcoholic solution in the ice chest penicillin loses its activity after 20 days while aureomycin maintains good stability for 60 days. At room temperature the alcoholic aureomycin solution still maintains good stability at 60 days, but penicillin becomes practically completely inactive after 3–4 days. Alcoholic and watery solutions of picromycin and terramycin in the ice chest and at room temperature both show quite good activity after 60 days.

An alcoholic solution of penicillin is too unstable for general use. M. S. S.

THE RECOVERY FACTOR AND ITS OPPOSITE IN TOXIC AND ALLERGIC SKIN DISEASES. W. Gahlen. (1952) *Derm. Wschr.*, **126**, 850.

The author uses mathematical formulae (borrowed from Schreus) to illustrate the relative importance of some factors in the pathogenesis of toxergic and allergic skin diseases.

He uses turpentine in oil in increasing strengths from 5% to study the toxergic type of reaction, and anaesthesin in vaseline from 1% for the allergic in five allergic individuals.

First he finds the concentration and time required to produce the earliest skin reaction in a normal individual. Repeated small concentrations take longer to produce a reaction (summation reaction) than the sum of the concentrations applied once. This heightening of tolerance he considers is due to a recovery factor.

In the normal individual increased concentration shortens the reaction time and reduced concentration prolongs it. In the allergic individual the reaction time in comparison is altered relatively little with variations in concentration, i.e., in allergy in contrast to normergy there is a factor which increases the speed and power of the reaction ; the reaction takes a relatively shorter time to develop, in response to relatively weaker concentrations. Mathematically this is expressed as follows :

$C \cdot t^n = K$; $n = 1$ summation reaction.
$C \cdot t^n = K$; $n < 1$ toxergic (normergic) reaction.
$C \cdot t^n = K$; $n > 1$ allergic reaction.
$C =$ concentration ; $t =$ time ; $K =$ constant. M. S. S.

CAUSES OF CUTTING OIL DERMATITIS. G. E. Morris and C. Maloof. (1952) *New Engl. J. Med.*, **247**, 440.

Experiments with oils which fluoresce under ultra-violet light showed that none of twenty-eight detergents freed the skin entirely from oil. The authors conclude that failure to remove oil completely is the main cause of oil dermatitis.

Contributory causes are the use of " wipe rags " which are supposed to be clean, but may in fact contain oil and grease, and antiquated machinery which sprays oil over the worker.

A. D. P.

EPIDERMAL REACTIONS TO REPEATED PATCH TESTS. F. R. Kogoj. (1952) *Acta allergol.*, **5**, 222.

Positive patch tests were obtained with various allergens in a series of 14 patients. After an unstated interval patches were re-applied on the same cases. In 6 cases the reaction was increased, in a further 6 it was the same and in 2 it was reduced. Similar tests were made with different allergens on 9 patients showing more than one sensitivity. H. T. H. W.

CLINICAL SENSITIVITIES TO GELATIN AND OTHER MEAT PRODUCTS. W. H. Hughes. (1952) *Acta allergol.*, **5**, 230.

Three cases are described illustrating sensitivity to meats and their derivatives. Two suffered from urticaria and one from asthma. Antibodies were demonstrated in the blood of a patient sensitive to gelatin and hyposensitization was successfully carried out. H. T. H. W.

EXPERIMENTAL STUDIES ON PITYROSPORON OVALE : ITS PATHOGENICITY AND ANTIGENIC CAPACITY. G. L. Rocha, C. Silva, A. O. Lima and M. Goto. (1952) *J. invest. Derm.*, **19**, 289.

Confirms the work (without acknowledgment) of Martin-Scott, who has already satisfactorily demonstrated that the pityrosporon gives no laboratory or experimental evidence of either pathogenicity or allergenic capacity. J. H. T. D.

INDUSTRIAL DERMATITIS. Mark Hewitt. (1951) *Lancet*, **2**, 1105.

From this study of 80 consecutive cases of industrial dermatitis he concludes that classification on an occupational or dermatological basis is unsatisfactory. The associated social, occupational and emotional disturbance seems to be an integral part if not a cause of the condition. Psychosomatic manifestations predominate, and the malady is often indistinguishable from an occupational neurosis. It is felt that the usual preventive measures are unlikely to be effective, but that a combined social, clinical and occupational approach to the problem of industrial dermatitis should be undertaken. R. H.